Journal of Cardiothoracic and Vascular Anesthesia 000 (2026) 1–8

Contents lists available at ScienceDirect

Journal of Cardiothoracic and Vascular Anesthesia

journal homepage: www.jcvaonline.com

Original Article

Indexed Delivery of Oxygen Predicts In-hospital Mortality and Morbidity in Reoperative Adult Cardiac Surgery Patients: A Retrospective Cohort Study

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Objectives: To evaluate the association between intraoperative indexed oxygen delivery (DO_2i) during cardiopulmonary bypass (CPB) and postoperative outcomes in patients undergoing reoperative cardiac surgery.
Design: Retrospective cohort study.
Setting: A tertiary academic cardiac surgery center.
Participants: A total of 343 patients who underwent reoperative cardiac procedures between January 2011 and January 2021.
Interventions: Patients were stratified by the median DO_2i threshold predictive of in-hospital mortality, identified using Youden's Index.
Measurements and Main Results: Median DO_2i was 300.8 ± 52.3 mL/min/m^2. In-hospital mortality was 14.6%. A median DO_2i <289.4 mL/min/m^2 predicted mortality (area under the curve = 0.756, sensitivity 78%, specificity 64%). Multivariable analysis showed that each 1 mL/min/m^2 decrease in DO_2i increased mortality risk by 1.6% (odds ratio [OR] 1.016, 95% confidence interval [CI] 1.007-1.024). DO_2i below the threshold was associated with a fourfold higher mortality risk (OR 4.12, 95% CI 1.18-9.49). After inverse-probability-of-treatment weighting, patients with low DO_2i had higher mortality (21.6% *v* 6.6%; p < 0.001), acute kidney injury (p = 0.042), cardiac morbidity (51.1% *v* 38.5%; p < 0.001), and prolonged ventilation (14.3% *v* 8.3%; p = 0.015).
Conclusions: Reduced intraoperative DO_2i was independently associated with increased risk of mortality and major morbidity following reoperative cardiac surgery. Incorporating continuous DO_2i monitoring and optimization into CPB management may improve outcomes in this high-risk population.

Key Words: mortality; cardiac surgery; redo; outcomes; perfusion

DESPITE ADVANCEMENTS IN PERIOPERATIVE CARE, mortality after cardiac surgery remains a concern, especially in complex or redo procedures. During cardiopulmonary bypass (CPB), oxygen delivery becomes entirely dependent on extracorporeal perfusion. Hence, indexed

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https://doi.org/10.1053/j.jvca.2026.01.002

oxygen delivery (DO_2i) has been identified as a critical determinant of tissue perfusion and organ function.[1-4]

Reoperative cardiac procedures expose patients to an inherent increased risk of hypoperfusion due to the increased physiological stress, prolonged operative times, and higher risk of complications such as bleeding, organ dysfunction, and hemodynamic instability. Therefore, maintaining an adequate DO_2i is even more crucial in these settings.[5,6]

Despite growing interest, the correlation between DO_2i and postoperative mortality remains underinvestigated. Pivotal studies suggest that insufficient DO_2i during CPB may lead to adverse outcomes such as acute kidney injury (AKI) and prolonged intensive care unit (ICU) stay.[1-4] Conversely, a recent meta-analysis showed that intraoperative hyperoxia is associated with worsening physiological and biochemical parameters.[7] Accordingly, this study was designed to evaluate whether low DO_2i during CPB is an independent predictor of 30-day mortality and perioperative complications in a selected cohort of patients undergoing reoperative cardiac surgery.

Methods

Study Population and Inclusion and Exclusion Criteria

This study was a retrospective analysis of prospectively collected data, including all patients who underwent a redo cardiac surgical procedure at the Department of Translational Medical Sciences, University of Campania "Luigi Vanvitelli" (Monaldi teaching Hospital) between January 2011 and December 2020. Inclusion criteria were age >18 years and a redo procedure. Exclusion criteria were aortic dissections, need for deep hypothermic circulatory arrest, ventricular assist device implantation, heart transplantation, and emergency surgery. Accordingly, from the original population of 388 consecutive patients, only 343 were included in the analysis.

The research protocol was approved by the local ethics and research committee (Monaldi Hospital Ethics and Research Committee protocol number 69/2022), which waived the need for informed consent.

CPB Management

Central cannulation was the primary strategy. In cases where peripheral cannulation was employed, the preferred sites included the right common femoral artery (107 patients), right axillary and/or subclavian artery (8 patients), and right common femoral vein (108 patients). CPB was most often initiated following sternotomy; however, in 99 patients, CPB was established prior to sternotomy due to hemodynamic instability (82 patients) or critical anatomical proximity to adjacent structures (17 patients: 15 right ventricular adhesion to the lower part of the sternum and 2 patent left internal mammary artery-left anterior descending artery grafts).

Once on CPB, the institutional protocols included CPB flow rates of 1.8 to 2.2 L/min/m^2 with a mean arterial pressure (MAP) of 50 to 70 mmHg. Crystalloid cardioplegia was the preferred choice (St. Thomas II: 306 patients, 89.2%; Custodiol: 33 patients, 9.6%); blood cardioplegia was used in only 2 patients (0.6%).

As per institutional protocol, arterial blood gas analyses were obtained at 20-minute intervals following initiation of CPB. All data were corrected for temperature, according to standard equations.[7] The estimates of oxygen delivery were calculated as follows:

$$DO2i\ [mL/min/m2] = 10 \times Pump\ Index\ [L/min/m2] \times Arterial\ O2\ Content\ [mL/100\ mL].$$

The target for DO_2i was at least 260 mL/min/m^2, which was achieved primarily by optimizing flow parameters and reinfusing blood sequestered in the operative field and, if necessary, by transfusing packed red cells (PRCs).[8,9]

To avoid potential bias arising from inadequate estimates of DO_2i associated with variation in cardiac output, only data for the time interval corresponding to the aortic cross-clamping were collected. Considering the fluctuation of DO_2i over time, the median value, rather than the nadir, was selected as the reference parameter for analyses.

Baseline Data and Study Endpoints

All definitions were selected prospectively as part of the original study design. The preoperative hemoglobin level was defined as the lowest documented hemoglobin value recorded at admission, during the preoperative period, or immediately before induction of anesthesia. The sex-based definition and grading scale of anemia complied with the statements by the World Health Organization (WHO).[10]

Glomerular filtration rate (GFR) was calculated with the Chronic Kidney Disease Epidemiology Collaboration formula (2021 version), and preoperative kidney function was graded accordingly; specifically, preoperative chronic kidney disease was defined as an estimated GFR ≤60 mL/min/1.73 m^2.[11]

In-hospital mortality was the primary target outcome. Secondary outcomes were the occurrence of AKI, cardiac morbidity, and permanent neurologic dysfunction.

For the postoperative AKI definition, the Kidney Disease: Improving Global Outcomes classification was referenced.[12] The main parameters considered in this study were creatinine and GFR, due to the heterogeneity of volume status and diuretic use in this setting, which may affect the relationship between renal function and urine output. Accordingly, urine output was not considered in the definition of AKI. To avoid the potential influence of postoperative events (low cardiac output, sepsis, effects of nephrotoxic agents, etc.) on the renal endpoint, for the specific purpose of this study, kidney function assessment was limited in time and defined as the difference between baseline serum creatinine concentration and the highest concentration during the first 3 postoperative days.

Cardiac morbidity was defined as the occurrence of a composite outcome including need for intra-aortic balloon pump,

extracorporeal membrane oxygenation, or infusion of continuous high-dose inotropic support for at least 24 hours postoperatively (namely, dobutamine infusion greater than 10 μg/kg/min or epinephrine added at any dose, as previously reported).[13]

Permanent neurologic dysfunction was defined as a persistent loss of neurologic function mainly caused by an ischemic event, with computed tomography scan evidence of brain injury, which was classified according to its extent, into focal (right or left hemispheric) or diffuse injury.[14]

Statistical Analysis

Continuous variables are reported as mean and standard deviation or median and interquartile range (IQR) if not normally distributed; categorical variables are reported as count and frequencies. Missing data were not imputed.

All preoperative and intraoperative variables whose differences were statistically significant in univariate analyses comparing discharged patients with those with in-hospital mortality recorded were entered into several multivariable logistic regression analyses using backward selection to identify predictors of in-hospital mortality. To avoid multicollinearity, variables with mathematical coupling were entered into separate models. In cases of intercorrelation, the best single independent predictor was selected.

The cutoff value of median DO_2i, which better predicted the occurrence of in-hospital mortality, was selected using the area under the curve and Youden's Index, which quantifies the optimal balance between sensitivity and specificity on a receiver operating characteristic curve, thus identifying the threshold value that best discriminates between individuals with and without a given outcome (Fig 1). Patients were thus stratified according to whether their median DO_2i fell below or above the identified cutoff for in-hospital mortality. Data were compared using unpaired *t*-tests, Mann-Whitney U-tests, and chi-square tests.

A nonparsimonious propensity score was built by multivariable logistic regression analysis, including preoperative and intraoperative variables judged a priori to be confounders or strong predictors of the outcome (age, sex, height, weight, baseline hemoglobin, baseline creatinine, left ventricular ejection fraction, pulmonary artery pressure, peripheral artery disease, chronic obstructive pulmonary disease, heart failure, diabetes, CPB institution before sternotomy, European System for Cardiac Operative Risk Evaluation [EuroSCORE] II), to estimate the propensity to record a median DO_2i below the identified threshold for mortality. The inverse probability of treatment weighting (IPTW)-average treatment effect (ATE) was used to adjust for imbalance in baseline characteristics between patients assigned to the two groups. To enhance robustness against model misspecification, a doubly robust augmented inverse probability weighting estimator was employed.

Covariate balance after weighting was assessed by calculating a weighted *t*-test for continuous variables, a weighted chi-square for dichotomous variables, and absolute standardized differences according to Austin and Stuart,[15] with values <0.10 considered optimal and <0.20 considered acceptable.[16,17] These tests were also used to assess differences in the occurrence of the study endpoints in the IPT-weighted analysis. The 95% confidence intervals (CIs) for the ATE were obtained using a bias-corrected bootstrap method with 1,000 resamples, providing robust inference that accounts for sampling variability and potential non-normality of the estimator. Statistical significance was set at an alpha level of 0.05. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Baseline characteristics of the study cohort are reported in Table 1. Notably, 199 patients (58.0%) had anemia at hospital

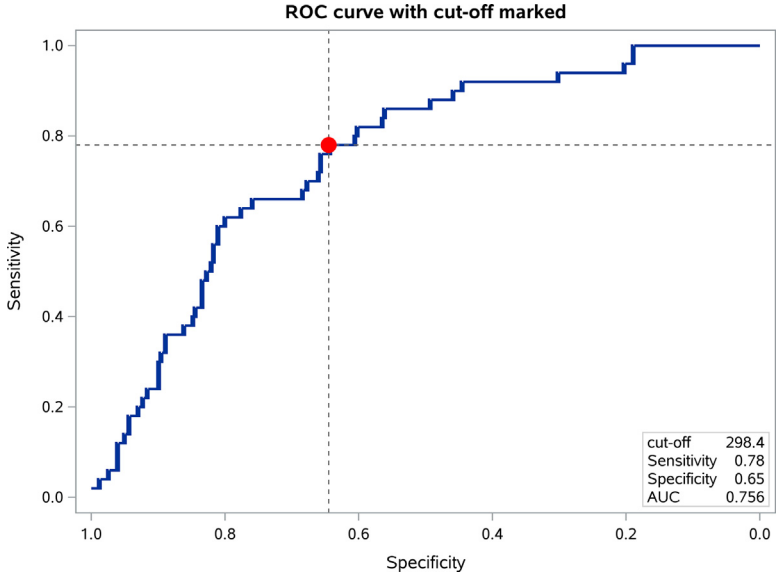

Fig 1. Receiver operating characteristic curve illustrating the threshold derivation.

Table 1
Baseline Details

	Overall	IPTW			
	N = 343	DO_2i <289.4 (SoW = 332.7)	DO_2i >289.4 (SoW = 347.7)	Std Diff.	p-Value
Age	62.3 ± 11.8	64.5 ± 18.1	61.9 ± 15.2	0.04	0.68
Female	170 (49.6)	181.1 (54.4)	183.9 (52.9)	0.03	0.68
Height	164.8 ± 9.6	164.5 ± 16.9	164.5 ± 10.8	0.00	0.99
Weight	73.1 ± 13.7	72.6 ± 22.8	73.0 ± 17.3	0.04	0.75
BSA	1.82 ± 0.20	1.81 ± 0.34	1.82 ± 0.25	0.03	0.78
BMI	26.9 ± 4.6	26.8 ± 7.0	27.0 ± 5.8	0.05	0.66
Hemoglobin	12.2 ± 2.3	12.1 ± 3.4	12.1 ± 3.1	0.01	0.94
Anemia	199 (58.0)	212.0 (63.7)	201.2 (57.9)	0.12	0.12
Anemia grade				0.02	0.82
No	144 (42.0)	120.7 (36.3)	146.5 (42.1)		
WNL (11.0-LNL)	137 (40.0)	153.2 (46.1)	135.3 (38.9)		
Mild (9.5-10.9)	13 (3.8)	14.1 (4.2)	9.4 (2.7)		
Moderate (8.0-9.4)	43 (12.5)	36.7 (11.6)	37.8 (10.9)		
Severe (6.5-7.9)	6 (1.8)	6.0 (1.8)	18.8 (5.4)		
Life-threatening (<6.5)	0	0	0		
Diabetes	71 (20.7)	71.6 (21.5)	66.6 (19.2)	0.06	0.44
Serum creatinine	1.0 ± 0.5	1.1 ± 0.9	1.1 ± 0.9	0.05	0.67
eGFR	79.2 ± 25.8	76.6 ± 39.1	77.3 ± 35.8	0.03	0.81
Chronic kidney disease	106 (30.9)	121.4 (36.5)	115.5 (33.2)	0.16	0.37
COPD	66 (19.2)	55.9 (16.8)	56.8 (16.3)	0.01	0.87
Extracardiac arteriopathy	21 (6.1)	19.0 (5.7)	28.3 (8.1)	0.10	0.21
LVEF	54.4 ± 8.4	54.5 ± 15.1	54.5 ± 10.5	0.00	0.99
PAPs	38.3 ± 14.9	39.3 ± 22.3	38.0 ± 2.5	0.09	0.44
Pathology				0.05	0.94
Endocarditis	47 (13.7)	45.9 (13.8)	48.5 (13.9)		
Failed repair/SVD	188 (54.8)	184.4 (55.4)	196.5 (56.5)		
Miscellaneous	108 (31.5)	102.3 (30.8)	102.7 (29.5)		
Preoperative intubation	1 (0.3)	1.1 (0.3)	0	0.08	0.29
Preoperative stroke	18 (5.3)	24.0 (7.2)	18.3 (5.3)	0.08	0.29
Previous CABG	43 (12.5)	56.0 (16.8)	47.5 (13.7)	0.14	0.25
Heart failure	66 (19.2)	62.8 (18.9)	60.0 (17.3)	0.04	0.58
Status				0.04	0.58
Elective	276 (80.7)	269.8 (81.1)	287.7 (82.7)		
Urgent	66 (19.3)	62.8 (18.9)	60.0 (17.3)		
EuroSCORE II	6.1 (3.7-10.3)	7.7 (4.5-13.0)	5.2 (3.0-8.7)	0.02	0.72

Abbreviations: BMI, body mass index; BSA, body surface area; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; EuroSCORE II, European System for Cardiac Operative Risk Evaluation II; LVEF, left ventricular ejection fraction; PAPs, systolic pulmonary artery pressure; SoW, sum of weights; Std Diff., standardized differences; SVD, structural valve deterioration; WNL, within normal limit.

admission (18.1% at least mild according to the WHO definition[16]), 106 (30.9%) had chronic kidney disease with an estimated GFR ≤60 mL/min/1.73 m^2, and 71 (20.7%) had diabetes. Only 66 patients (19.3%) were operated on urgently, namely, 31 (47.0%) for valve dysfunction, 20 (30.3%) for endocarditis, and 15 (22.7%) for other indications. Accordingly, the EuroSCORE II predicted an average mortality risk of 8.4% (median 6.1, IQR 3.7%-10.3%).

During CPB, the median DO_2i was 300.8 ± 52.3 mL/min/m^2, and the mean nadir hemoglobin was 7.9 ± 1.4 g/dL. One hundred and forty-two patients (41.4%) required red blood cell transfusion during CPB, with an average of 1.0 ± 1.5 PRC units transfused (Table 2). Fifty patients (14.6%) died during hospitalization. Postoperative AKI occurred in 184 patients (53.6%), with 41 patients (12.0%) requiring renal replacement therapy (Table 3). Cardiac morbidity occurred in 145 patients (42.3%), with the need for high-dose inotropic infusion accounting for the majority of the cases (139 patients, 40.5%). A total of 36 patients (10.5%) required prolonged mechanical ventilation, and 10 (2.9%) experienced a stroke. Median ICU stay was 3 days (IQR 2-5) with an overall median hospital length of stay of 14 days (IQR 8-21).

The cutoff value for median DO_2i that best predicted in-hospital mortality was set at a median DO_2i <289.4 mL/min/m^2, according to Youden's Index (area under the curve 0.756, 95% CI 0.689-0.823; sensitivity 0.78, specificity 0.64). Multivariable analysis revealed that any unit decrease in DO_2i was associated with a 1.6% increased risk of in-hospital mortality (odds ratio [OR] 1.016, 95% CI 1.007-1.024). A median DO_2i of lower than 289.4 mL/min/m^2 predicted a fourfold increased risk of mortality (OR 4.119, 95% CI 1.179-9.489).

When patients were stratified by median DO_2i value (below or above the identified cutoff), those in the lower DO_2i group had a higher risk profile, as reflected by a greater median EuroSCORE II (7.7% *v* 5.2%; $p < 0.001$). They also underwent longer CPB and cross-clamping time, required more

Table 2
Operative Details and Intraoperative Outcomes

	Overall	IPTW		
	N = 343	DO_2i <289.4 (SoW = 332.7)	DO_2i >289.4 (SoW = 347.7)	p-Value
Presternotomy CPB	99 (28.9)	97.6 (29.3)	96.8 (27.9)	0.67
Peripheral arterial cannulation	115	110.4 (33.2)	109.0 (31.5)	0.37
Peripheral venous cannulation	108	104.4 (31.4)	102.9 (29.7)	0.64
CPB, min	153.6 ± 95.5	162.2 ± 115.1	137.6 ± 112.0	0.005
XCT, min	90.4 ± 45.2	95.8 ± 74.1	84.4 ± 46.9	0.017
CPB >180 min	101 (29.5)	126.1 (37.9)	65.7 (19.0)	<0.001
Length of surgery	318.4 ± 95.7	331.7 ± 155.8	295.4 ± 102.5	<0.001
Median DO_2i (range)	300.8 ± 52.3 (159.4-550.3)	259.2 ± 35.7 (159.4-289.0)	326.0 ± 46.3 (289.8-550.3)	<0.001
Median DO_2i < critical value	142 (41.4)	-	-	-
Median CI	2.4 ± 0.3	2.4 ± 0.4	2.5 ± 0.3	<0.001
Nadir Hb	7.9 ± 1.4	7.1 ± 1.2	8.4 ± 1.5	<0.001
Nadir Hct	24.0 ± 4.2	21.6 ± 3.7	25.4 ± 4.6	<0.001
PRC during CPB	1.0 ± 1.5	1.3 ± 2.6	0.8 ± 1.6	0.002
PRC after CPB	0.6 ± 1.1	0.9 ± 2.4	0.4 ± 1.0	<0.001
PRC total	2.2 ± 2.7	2.8 ± 4.4	2.0 ± 3.2	0.013

Abbreviations: CI, cardiac index; CPB, cardiopulmonary bypass; DO_2i, indexed oxygen delivery; Hb, hemoglobin; Hct, hematocrit; IPTW, inverse probability of treatment weighting; PRCs, packed red cells; XCT, cross-clamping time.

transfusions, and experienced worse hospital outcomes. Notably, this group showed a significantly higher incidence of renal, cardiac, and respiratory complications, prolonged hospitalization, and elevated in-hospital mortality (26.8% *v* 6.0%; $p < 0.001$). Full comparisons of baseline and intraoperative details, as well as postoperative outcomes, are reported in Supplementary Tables 1 and 2.

IPTW balanced the preoperative risk profiles (Table 1). Nonetheless, weighted analyses confirmed prolonged surgery duration, lower average median DO_2i, hemoglobin, and hematocrit, as well as higher transfusion rates (Table 2). When the primary outcome was considered, IPTW analysis confirmed an increase in in-hospital mortality in the lower DO_2i cohort. Using a doubly robust augmented inverse probability weighting model, a median DO_2i below the identified threshold was associated with a higher risk of in-hospital death. The estimated ATE was 0.151 (95% CI 0.057-0.254), indicating a 15.1% increase in postoperative mortality among patients

Table 3
In-hospital Results

	Overall	IPTW			
	N = 343	DO_2i <289.4 (SoW = 332.7)	DO_2i >289.4 (SoW = 347.7)	Weighted Risk Diff.* (95% CI)	p-Value
Peak creatinine	1.5 ± 0.8	1.5 ± 1.2	1.4 ± 1.2	0.06 (−0.10-0.23)	0.68
Nadir eGFR	63.4 ± 38.7	60.7 ± 55.5	64.7 ± 54.9	−0.12 (−0.40-0.17)	0.35
Acute kidney injury				−0.04 (−0.19-0.10)	0.042
No	159 (46.4)	143.3 (43.1)	160.6 (46.2)		
1	105 (30.6)	121.5 (36.5)	110.8 (31.9)		
2	30 (8.8)	13.4 (4.0)	29.8 (8.6)		
3	49 (14.3)	54.5 (16.4)	46.5 (13.4)		
CVVH	41 (12.0)	49.2 (14.8)	40.4 (11.6)	0.03 (−0.02-0.08)	0.22
Cardiac morbidity	145 (42.3)	170.1 (51.1)	133.8 (38.5)	0.12 (0.05-0.20)	<0.001
ECMO	9 (2.6)	13.8 (4.2)	3.0 (0.9)	0.03 (0.01-0.06)	0.006
IABP	21 (6.1)	29.9 (9.0)	12.8 (3.7)	0.05 (0.02-0.09)	0.005
High-dose inotropes	139 (40.5)	166.8 (50.1)	127.2 (36.6)	0.14 (0.06-0.21)	<0.001
Prolonged mechanical ventilation (≥72 h)	36 (10.5)	47.5 (14.3)	29.0 (8.3)	0.06 (0.01-0.11)	0.015
Tracheostomy	10 (2.9)	10.8 (3.2)	9.0 (2.6)	0.01 (−0.02-0.03)	0.61
Readmission to ICU	12 (3.5)	7.7 (2.3)	16.4 (4.7)	−0.02 (−0.05-0.01)	0.17
Bleeding requiring reoperation	11 (3.2)	7.9 (2.4)	10.2 (2.9)	−0.01 (−0.03-0.02)	0.65
Postoperative stroke	10 (2.9)	13.3 (4.0)	10.4 (3.0)	0.01 (−0.02-0.04)	0.47
Median ICU length of stay	3 (2-5)	4 (2-6)	3 (2-5)	0.09 (−0.07-0.26)	0.09
Median postoperative stay	14 (8-21)	15 (9-22)	13 (8-20)	0.04 (−0.18-0.28)	0.91
In-hospital death	50 (14.6)	71.7 (21.6)	23.0 (6.6)	0.15 (0.10-0.20)	<0.001

Abbreviations: AKI, acute kidney injury; CVVH, continuous venovenous hemofiltration; eGFR, estimated glomerular filtration rate; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; ICU, intensive care unit; IPTW, inverse probability of treatment weighting.

* Computed as DO_2i <289.4-DO_2i >289.4.

whose median DO_2i fell below the threshold compared with those above it. Similarly, AKI and cardiac morbidity occurred more frequently (51.1% *v* 38.5%; $p < 0.001$, with significant differences for each element of the composite endpoint), as well as the need for prolonged mechanical ventilation. On the other hand, the median hospitalization length was comparable between the two groups (Table 3). Propensity score-adjusted multivariable models confirmed the strong association between low oxygen delivery and in-hospital mortality (Fig 2).

Discussion

Key Findings

This study demonstrates that low intraoperative DO_2i is a strong independent predictor of in-hospital mortality after reoperative cardiac surgery (OR 4.119, 95% CI 1.179-9.489), along with other known risk factors such as renal function indexes, left ventricular ejection fraction, underlying pathology (especially endocarditis), diabetes, urgency, EuroSCORE II, duration of surgery, and need for transfusions of PRCs. These data are consistent with a retrospective analysis of 1,700 patients published by Bianco and coworkers, who identified reoperative cardiac surgery as a strong predictor of morbidity and mortality.[18]

Both inadequate and excessive oxygen delivery during CPB have been implicated in postoperative organ dysfunction. Insufficient oxygenation can lead to tissue hypoxia, contributing to complications such as AKI, neurologic impairment, and prolonged recovery.[1-3,5] However, emerging evidence also indicates that hyperoxia during CPB may be detrimental, promoting oxidative stress, inflammation, and microvascular injury.[7,19]

Accordingly, the current observations align with prior pivotal studies that identified low DO2i as a key trigger of organ hypoxemia, emphasizing that inadequate oxygen delivery during CPB can precipitate cellular hypoxia and induce subsequent organ dysfunction.[1-3,5] In particular, Ranucci et al. and De Somer et al. reported that the lowest oxygen delivery, with critical values of 272 mL/min/m^2 and 262 mL/min/m^2, respectively, was independently associated with postoperative AKI.[1,3] The current results further substantiate the association between reduced intraoperative DO_2i and the development of AKI, with the relationship remaining robust following adjustment through IPTW. However, the current authors may argue that an inadequate oxygen supply during CPB translates into a hypoxic injury that is not only confined to the renal medulla but also significantly impairs the whole body.[20] This might be even more pronounced in patients undergoing redo surgery, whose heightened vulnerability may be explained by their inherent complexity, longer CPB durations, and amplified inflammatory responses, all contributing to increased physiological stress and tissue hypoxia.[21] In the current analysis, 101 patients (29.5%) underwent CPB lasting more than 180 minutes, a condition commonly referred to as prolonged CPB.[4] It may be inferred that the longer the CPB duration, the greater the patient's exposure to risks associated with hypoperfusion and an amplified inflammatory response. Accordingly, an optimal median DO_2i threshold of 298.4 mL/min/m^2 was identified for predicting in-hospital mortality, demonstrating acceptable discriminative ability, with a sensitivity of 78% and specificity of 64% (area under the curve 0.756, 95% CI 0.689-0.823). In the unweighted analysis, patients in the lower

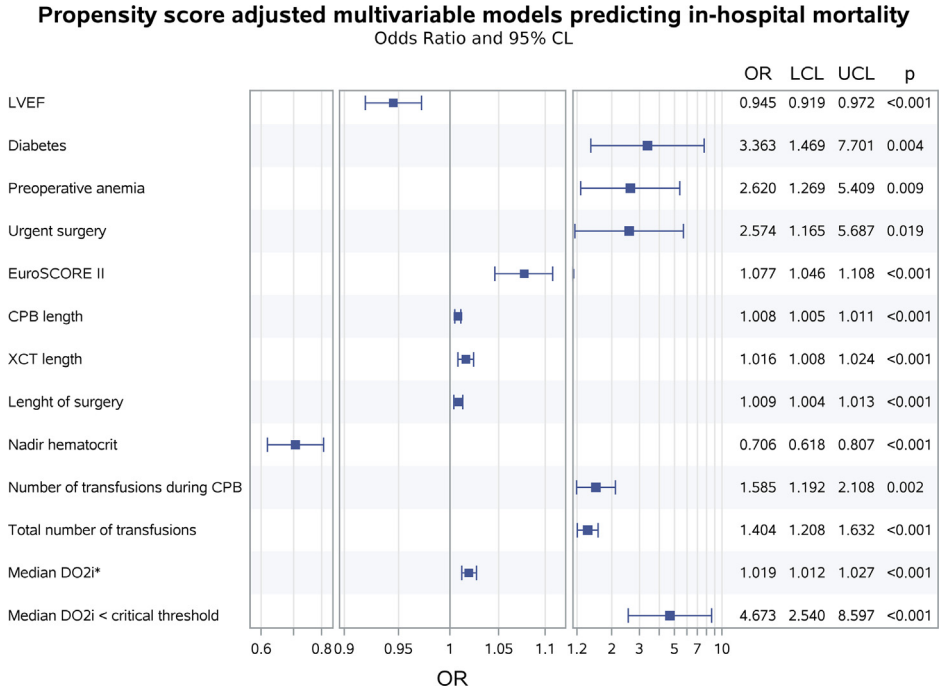

Fig 2. Propensity score-adjusted multivariable models of in-hospital mortality. *Intended as 1.9% increased odds per unit decrease in median DO_2i. CPB, cardiopulmonary bypass; DO_2i, indexed delivery of oxygen; LVEF, left ventricular ejection fraction; XCT, cross-clamping time.

DO_2i group exhibited a baseline clinical profile characterized by a higher intrinsic risk for postoperative morbidity and mortality. However, even after effective adjustment for baseline confounders using IPTW, a median DO_2i <298.4 mL/min/m^2 was associated with prolonged CPB times and remained independently associated with significantly worse outcomes. Specifically, these patients experienced higher in-hospital mortality (weighted rates: 21.6% *v* 6.6%; $p < 0.001$), an increased incidence of AKI ($p = 0.042$), greater cardiac morbidity (weighted rates: 51.1% *v* 38.5%; $p < 0.001$), and a higher rate of prolonged mechanical ventilation (weighted rates: 14.3% *v* 8.3%; $p = 0.015$). In the doubly robust analysis, a median DO_2i below the identified mortality threshold was associated with a substantially higher probability of postoperative death, with an ATE of 0.151. This suggests that even after accounting for both preoperative and intraoperative confounders, patients exposed to lower oxygen delivery had an approximately 15% greater absolute risk of mortality. These findings are consistent with those reported by Magruder et al., who demonstrated an independent association between reduced intraoperative DO_2i and an increased incidence of postoperative complications[22] and support the hypothesis that maintaining adequate DO_2i during surgery may have a clinically meaningful impact on survival outcomes.

Limitations

Several studies identified cumulative time spent under the ischemic threshold, rather than a single record, as a risk factor for AKI.[23,24] One major limitation of the current study is that DO_2i was not continuously recorded; therefore, the continuous dynamic changes in flow-dependent parameters could not be accurately evaluated. Therefore, the recorded DO_2i might not accurately reflect the exposure time to low oxygen delivery. This was partially addressed by selecting the median value during cross-clamping time. Second, this study suffers from all the limitations of a single-center, retrospective study. On the one hand, this guarantees uniformity in definition and data collection, but center-specific biases might remain unbalanced in the analysis. Third, although some restrictions in inclusion and exclusion criteria have been applied, the sample of all-comer redo patients includes a wide range of preoperative risk profiles, which may hamper the drawing of firm conclusions on the prespecified endpoints. Fourth, the derived cutoff threshold alone may not fully account for the occurrence of poorer postoperative outcomes, which are well recognized as multifactorial.

Conclusions

These findings underscore the prognostic relevance of intraoperative DO_2i levels during CPB, particularly in high-risk populations such as reoperative cardiac surgery patients. Even after adjustment for baseline characteristics, a median DO_2i below the identified threshold remained independently associated with worse postoperative outcomes, including increased mortality, organ dysfunction, and prolonged recovery. This highlights an opportunity for refining perfusion strategies, potentially incorporating DO_2i-guided protocols to tailor CPB management. Future prospective studies are warranted to validate these findings and to explore whether interventions aimed at optimizing DO_2i can improve short- and long-term patient outcomes. Collectively, the current results advocate for a paradigm shift toward more individualized oxygen delivery monitoring during cardiac surgery, especially for high-risk populations such as patients undergoing redo operations.

Funding

This research received no external funding.

Institutional Review Board Statement

The research protocol was approved by the local ethics and research committee, which waived the need for informed consent (Vincenzo Monaldi Hospital Ethics and Research Committee protocol number 69/2022).

Informed Consent Statement

Patient consent was waived due to the study's observational design.

Data Availability Statement

The data presented in this study are available on reasonable request from the corresponding author.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Antonino Salvatore Rubino: Writing – original draft, Methodology, Formal analysis, Conceptualization. **Luca Salvatore De Santo:** Writing – original draft, Validation, Methodology, Conceptualization. **Michele Torella:** Resources. **Antonio Pio Montella:** Data curation. **Caterina Golini Petrarcone:** Data curation. **Lucrezia Palmieri:** Data curation. **Denise Galbiati:** Data curation. **Antonio Pisano:** Writing – review & editing. **Federico Pappalardo:** Writing – review & editing. **Marisa De Feo:** Supervision.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.jvca.2026.01.002.

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